



(12) 发明专利申请公开说明书

[21]申请号 93111461.6

[51]Int.Cl³

A61K 35/78

[43]公开日 1994年12月28日

[22]申请日 93.6.23

[71]申请人 湖南医科大学附属第二医院医药技术开
发公司

地址 410011湖南省长沙市人民路156号

[72]发明人 赵绪元 黄波 许树梧 陈奉治

[74]专利代理机构 湖南省专利服务中心
代理人 程桂兰

A61K 9/68

//(A61K 35/78,31:415)

RECORD COPY
CENTRAL FILE

说明书页数:

附图页数:

[54]发明名称 健齿香口胶及其制作方法

[57]摘要

健齿香口胶是选用对口腔厌氧菌有显著抑制作用的西药甲硝唑或洗必泰盐与中药两面针或入地金牛为有效成份,同时添加适量由糖、食用胶姆等组成的辅料,采用一定方法制作而成。临床试用证明本品对缓解口腔炎症、清洁口腔、降低牙菌斑效果明显,特别是对牙残根、缺失牙者、口臭患者作用显著,同时对龋齿病也有一定防治作用,临床主要适用于各年龄阶层的口腔疾病(牙龈炎、牙周炎、口臭)的预防和治疗,是一种大众化的新型保健食品。

(BJ)第 1456 号

PATENTS SUMMARY

04/23/99

Page 1

Country : China

Patent #: 1,096,699 A

Index#: 5473

Inventor: Yang Zhe

Issue Date: 12/28/94

Assignee: Hong Oi Pharmaceutical Factory Date of Application: 01/07/94

Title:

ANTICARIES CHEWING GUM AND ITS MANUFACTURING METHOD

Desc.:

An anticaries chewing gum containing as the active ingredient the dried extract of magnolia bark (*Cortex magnoliae officinalis*) and the manufacturing method are claimed. The extract can be substituted by extracts of *Magnolia abovata*, rhizomes of Chinese goldthread (*Coptis chinensis*) and Chinese gall. The gum also contains dietary fiber and microcapsules of stevia sweetener. The gum cleans the teeth, kills bacteria and prevents dental caries.

Key Words:

10 CHEWING GUM
17 Sugarless (Gum)
20 Anticaries/Antiplaque (Gum)
25 Pharmaceutical
177 Stevia Sweeteners
466 Spices/Herbs
467 Pharmaceutical Agents
489 Dietary Fiber
504 Mixing/Gum Manufacture
525 Chemical Synthesis/Preparation
574 Health Benefit
600 ORAL HEALTH
601 Anticaries/Antiplaque/Anticalculus
603 Antibiotic
605 Non-cariogenic Sweetener or Product
799 Other Company/Institution
839 China

Don Hank Translations/ 2929 Columbia Avenue/ Lancaster, PA 17603/ Phone: 717-390-8894/ Fax: 717-390-8790

RECORD COPY
CENTRAL FILE

ANTICARIES CHEWING GUM AND
ITS MANUFACTURING METHOD
[Fangqu kouxiangtang jiqi zhizuo fangfa]

CN 1,096,699

5473

54743

10

17

20

25

177

466

467

489

504

525

574

600

601

603

605

799

839

Translated from Chinese

QB/qb

6013
7/9/97

[19] Patent Office of the People's Republic of China

[11] Laid-Open number: CN 1096699A

[12] LAID-OPEN PATENT APPLICATION

[21] Application number: 94110006.5

[43] Laid-Open date: December 28, 1994

[51] Int.Cl⁵ A61K 35/78

A61K 35/78

9/68 A23G 3/30

[22] Application date: January 7, 1994

[71] Applicant: Hong Qi (Red Flag) Pharmaceutical Factory of ShenYang City

Address: No.36, Xinlong Road, DaDong district, ShenYang City, Liaoning Province 110041

[72] Inventors: Yang Zhe

[74] Agency: Patent Agency of ShenYang City

Agent: Diao Peide, Jia Shiming

Number of pages in Specification :

Number of pages of Figures:

[54] Title: ANTICARIES CHEWING GUM AND ITS MANUFACTURING METHOD

[57] Abstract: *The invention relates to an anticaries chewing gum and to its manufacturing method. The materials used for this invention include extract of magnolia bark (Cortex magnoliae officinalis), microcapsules of stevia sweetener, dietary fiber, fat, gum base and the other usual chewing gum ingredients. The chewing gum product can be made by using a mixer to blend these materials to homogeneity, then grinding and extruding the mixture, cutting and packaging. The manufacturing method is straightforward and the chewing gum product is convenient to use. Besides the same advantages of conventional chewing gum, this inventive product has the characteristics of cleaning the teeth, killing bacteria and preventing dental caries.* ✓

(BJ) No. 1456

CLAIM

1. Chinese medicine-containing anticaries chewing gum, characterized by the fact that it contains as constituents 0.02-7.72 parts extract of magnolia bark (*Cortex magnoliae officinalis*), 10-70 parts dietary fiber, 0.2-3 parts fat, 0.16-2 parts microcapsules of stevia sweetener, and 15-26 parts gum base.

2. Anticaries chewing gum in accordance with Claim 1, characterized by the fact that it contains as constituents 0.14 parts of the extract of magnolia bark (*Cortex magnoliae officinalis*), 30 parts dietary fiber, 2.5 parts fat, 0.8 parts microcapsules stevia sweetener, and 25 parts gum base material.

3. Anticaries chewing gum in accordance with Claim 1 or 2, characterized by the fact that the extract of magnolia bark (*Cortex magnoliae officinalis*) can be substituted by: extract of *Magnolia obovata*, extract of the rhizomes of Chinese goldthread (*Coptis chinensis*) and Chinese gall.

4. Manufacturing method for the anticaries chewing gum in accordance with Claim 1 or 2, characterized by the process wherein a mixture is prepared according to a recipe consisting of 0.02-7.72 parts extract of magnolia bark (*Cortex magnoliae officinalis*), 10-70 parts dietary fiber, 0.2-3 parts fat, 0.16-2 parts microcapsules of stevia sweetener, and 15-26 parts gum base, by a procedure wherein the gum base material, dietary fiber and fat are placed in a mixer and blended to homogeneity, the extract of magnolia bark, microcapsules of stevia sweetener and the other ingredients conventionally used in making chewing gum are added, and the final product is obtained from this mixture by extruding, cutting and packaging.

5. Method in accordance with Claim 4, characterized by a processes for preparing the extract of magnolia bark (*Cortex magnoliae officinalis*) wherein ethanol or methanol are added to the powdered magnolia bark, the mixture is extracted by heating and refluxing, and the extract is obtained from the resulting liquid by cooling, filtering, and concentrating to dryness.

6. Method in accordance with Claim 4, characterized by process for preparing the extract of magnolia bark (*Cortex magnoliae officinalis*) wherein the powdered magnolia bark is alkalized and filtered, the filtrate is acidified with acid, refiltered, and the sediment is introduced into ethanol or methanol to dissolve; the liquid is refiltered, and the ethanol or methanol solution is collected and concentrated to dryness to obtain the extract.

7. Method in accordance with Claim 4, characterized by a process for preparing the extract of magnolia bark (*Cortex magnoliae officinalis*) wherein the magnolia bark is ground into powder, water is added to the powder at a mixing ratio of magnolia bark to water of 1: (5-10), and the system is boiled twice, after which the decoctions of the first and second boil are combined, and the extract is obtained by filtering the decoctions and concentrating to dryness.

8. Method in accordance with Claim 4, characterized by a process for preparing microcapsules of stevia sweetener wherein ethyl cellulose and stevia sweetener are placed in a sandwich structured enamel jar at a mixing ratio of (0.01-0.1):1; the mixture is stirred with heating until the temperature reaches 75-85°C and the ethyl cellulose dissolves; the system is cooled to room temperature, and the stevia sweetener capsules are filtered out and washed two or three times with cyclohexanone, then dried under vacuum to obtain the stevia sweetener microcapsules.

9. Method in accordance with Claim 4, characterized by a process wherein the dietary fiber is prepared by grinding to powder and sieving the powder with a sieve of at least 100 mesh.

10. Method in accordance with Claim 4, characterized by the fact that gum base it contains is conventional chewing gum base.

SPECIFICATION

ANTICARIES CHEWING GUM AND ITS MANUFACTURING METHOD

This invention concerns a chewing gum which contains Chinese medicine and is capable of preventing dental caries. It also has complementary functions of oral cleansing, suppression of bad breath and treatment of various oral inflammations.

Caries is a common mouth disease frequently encountered today. According to statistics of World Health Organization (WHO), caries is the disease ranking next after cardiovascular diseases and

cancer in term of injury to humans. In China, 56.6% of children aged 1-13 suffer from caries. Many adults and elderly people also suffer from this disease. Therefore medical workers are becoming increasingly concerned with improvements in caries treatment. It is generally recognized that *Streptococcus mutans* is responsible for caries. Some research has already been made on anticaries drugs. Antibiotics such as penicillin, ilotycin and cyclomycin are efficacious in preventing caries. However, these drugs can upset the balance of bacteria colonies in the oral cavity and the intestines. This unbalance in turn can cause various diseases. Since the advent of chewing gum, people have regarded chewing gum as the health care food for improving oral hygiene and welcome it for its merits. Because chewing gum is sticky and withstands chewing, it can rub away tartar and plaque on the teeth. The gum base has a massage action on teeth, promotes the health of the periodontium, strengthens teeth and tones facial muscles. The gum base of chewing gums now sold on the market contains a certain amount of cleaning agent and bactericidal agents such as chlorhexidine. These agents act to inhibit oral inflammation and suppress bad breath. Chlorhexidine is a broad spectrum anionic disinfectant. It can inhibit and kill many bacteria, but *Streptococcus mutans* and lactobacillus are insensitive to it. Long term and unlimited use of Chlorhexidine can cause side effects such as desquamation of oral mucosa and color changes in tongue, teeth and silicate dental fillings. The pathogen is capable of fermenting sugar and producing organic acids such as lactic acid which in turn can gradually lead to decalcification of teeth and hence to cavities. At this point, infection is very likely to occur, leading to impaired health.

The purpose of this invention is to offer a Chinese medicine-containing anticaries chewing gum. The inventive product is convenient for use and its manufacturing method is straightforward. Besides affording the same advantages as conventional chewing gum such as tooth strengthening and dental care, it is characterized by an outstanding dental cleaning, bactericidal and caries preventive action.

This purpose is achieved as follows.

The anticaries chewing gum contains the following ingredients: 0.02-7.72 parts extract of magnolia bark, 10-70 parts dietary fiber, 0.2-3 parts fat, 0.16-2 parts microcapsules of stevia sweetener, and 15-26 parts gum base. The preferred recipe is: 0.14 part extract of magnolia bark, 30 parts dietary fiber, 2.5 parts fat, 0.8 parts microcapsules of stevia sweetener, and 25 parts gum base.

The manufacturing method is as follows: Introduce the gum base, dietary fiber and fat into a mixer and mix to homogeneity. Add the extract of magnolia bark, microcapsules of stevia sweetener and other usual ingredients of chewing gum. Then make the final product by extrusion, cutting and packaging.

This inventive chewing gum can improve oral hygiene in the same way as ordinary chewing gum because it contains as a vehicle the same gum base as that contained in popular chewing gums. As the inventive characteristic we replaced part of granulated sugar with stevia sweetener microcapsules and dietary fiber, thereby improving the flavor of the chewing gum. Conventional chewing gums may contain, for example, antibiotics such as chlorhexidine as anticaries medication, which have side effects. This invention utilizes extract of magnolia bark instead, thereby effectively avoiding the side effects that exist with conventional chewing gum. Although magnolia bark has not yet been used in practice as an anticaries medicine, laboratory experiments show that hinokiol and magnolol as active principles quickly and effectively kill *Streptococcus mutans*. The inventive gum has little toxicity as an oral medication, and colibacilli are insensitive to it; therefore it will not cause disturbances in the enteric flora even when used for an extended period. For both honokiol and magnolol, the minimum inhibitory concentration (MIC) is 6.3 µg/mL, the minimum bactericidal time 5 minutes, and the minimum bactericidal concentration (MBC) 50-75 µg/mL. Stevia sweetener is an intense natural sweetener. It is an ideal substitute for sucrose. By reducing the quantity of sucrose, one can avoid excessive organic acid production from sugar under the influence of cariogenic bacteria, thus avoiding damage to the teeth. Experiments show that stevia sweetener cannot be used as the carbon source by

Streptococcus mutans to make acid or insoluble polysaccharides, so this invention utilizes stevia sweetener to improve the anticaries action of chewing gum. The stevia sweetener can be transformed to microcapsules and added to gum base. By designing the capsules for gradually release over 5 to 10 minutes, we achieve a longer chewing time than that of ordinary chewing gum. For ordinary chewing gum, the flavor and taste deteriorate after the gum is chewed for more than 2 minutes. This invention remedies this shortcoming and is characterized by a sweet pleasant taste and enduring flavor. The dietary fiber, which swells with the moisture in the mouth, provides friction for better contact between the teeth and the chewing gum. With the friction feature of dietary fiber and the adhesive feature of gum base, tartar and plaque can be removed and better tooth cleaning action achieved. Thanks to the presence of the dietary fiber, the bacteria cannot take advantage of the granulated sugar in the chewing gum to produce acid. This finding was unexpected.

According to an investigation performed by the Food Hygiene Inspection Office of Liaoning Province as well as clinical observations, the inventive chewing gum has outstanding action in terms of caries prevention and is free of toxic side effects. Its structure is as follows:

1. SAFETY

1) Acute toxicity test (rat and mouse)

Lethal dose of 50% (LD50) g/kg >21.50. Rated non toxic.

2) Toxicity accumulation test on rats.

After application of toxicant for 20 consecutive days, all mice survived. No mouse was intoxicated. $K > 5$. Belong to the category of weak accumulation;

3) Micronucleus test on mouse marrow: no mutagenicity observed in the test mice.

4) Mutagenicity test on mouse sperm: no mutagenicity observed in the test mice.

5) Salmonella/microsome mutagenicity test. The result is negative.

2. EFFICACY

The minimum inhibitory concentration at which the anticaries chewing gum inhibits *Streptococcus mutans* is 0.05 g/mL.

The minimum bactericidal concentration at which the anticaries chewing gum kills *Streptococcus mutans* is 0.25 g/mL.

As a clinical experiment, we selected 186 first year primary school pupils and randomly divided them into two groups. One group was the test group, and the other the control group. According to the protocol, each subject was to chew one stick of chewing gum for 5-10 minutes after each meal, i.e., breakfast, lunch and dinner. The test criteria were: incidence of new caries and incidence of caries in progress.

TEST RESULTS (1). STATISTICS OF NEW CARIES OCCURRENCE

Group	Number of teeth observed	Number of teeth with new caries	Incidence of new caries
Test group	1660	15	0.9%
Control group	1810	248	13.7%

There is a major difference between the two groups ($P < 0.01$), indicating that anticaries chewing gum reduces the incidence of new caries.

(2) STATISTICS OF CARIES IN PROGRESS:

Group	Number of teeth observed	No. of teeth with new caries [sic]	Incidence of new caries [sic]
Test group	417	13	3.11%
Reference group	385	184	47.79%

There is a major difference between the two groups ($P < 0.01$), indicating that anticaries chewing gum arrests the development of caries.

3. QUALITY CONTROL TARGET

Item	Target
Arsenic (AS) mg/kg	< 0.5
Lead (Pb) mg/kg	< 1.0
Copper (Cu) mg/kg	< 10.0
Total number of bacteria/g	< 500
Total no. of enteric bacteria colonies/100 g	< 30
Number of pathogenic bacteria	not available
Amount of drug (calc. based on magnolol)	> 0.14%

Following is a detailed description on the basis of embodiments:

First the ingredients are prepared from raw materials, then compounded according to the recipe.

The ingredients are prepared as follows:

1. Preparation of magnolia bark extract

Grind magnolia bark (*Cortex magnoliae officinalis*) into powder. Add ethanol or methanol (choose the concentration as required. Normally 95% or 50% is the optimum concentration). Proceed with heating and reflux extraction. Prepare the extract by cooling and filtering the resulting liquid and concentrating to dryness.

1.2. Grind magnolia bark into powder. Alkalize and filter the powdered magnolia bark, acidify the filtrate with acid, filter, place the sediment in ethanol or methanol to dissolve (use the same concentration level as above), filter, collect the ethanol or methanol and concentrate to dryness to obtain the extract.

1.3. Grind magnolia bark into a powder, place in water at a ratio of magnolia bark to water of 1: (5-10) and boil twice. Combine the decoctions from the 2 boilings and obtain the extract by filtering and concentrating the decoctions to dryness.

1.4. The extract of magnolia bark can be substituted by extract of *Magnolia obovata*, extract of Chinese goldthread (*Coptis chinensis*) rhizomes and Chinese gall.

2. Preparation of stevia sweetener microcapsules

Place ethyl cellulose and stevia sweetener at a ratio of (0.01-0.1):1 (0.02:1 is the preferred ratio) into a sandwich structured enamel jar (with mixer and cooler) and add polyolefins as an accelerator to

speed up the formation of capsules. Heat the mixture until the temperature reaches 75-85°C and until the ethyl cellulose dissolves. Cool to room temperature and filter out the stevia sweetener capsules; wash them two or three times with cyclohexanone, and dry under vacuum to obtain the microcapsules of stevia sweetener.

Depend on the requirement, the flavoring material can also be encapsulated before being put into gum base.

3. Preprocessing the dietary fiber

The dietary fiber can be processed to a fineness level such that its roughness cannot be perceived. The dietary fiber can be ground into a powder and the powder sieved to obtain the dietary fiber ingredient as long as the mesh of the sieve used is not less than 100.

4. Preprocess the gum base material

Use a gum base identical to that used for ordinary chewing gum, and use a conventional method for cutting and softening the gum base and preparing it for use.

5. Selection of fat

By adding the proper amount of fat, one can prevent the dietary fiber from dissolving when the dietary fiber absorbs saliva and swells. By so doing one can also confer appropriate elasticity to the chewing gum. Vegetable oils are preferred in this case. For example, these oils can be 20-45 °C cocoa butter, palm butter, palm nut oil, coconut oil, etc.

6. Preparation of other ingredients

In this invention, the other ingredients are the same as in conventional chewing gum. For example, a small amount of granulated sugar and glucose syrup are added as adhesives and sweeteners, glycerol is added as a humectant, and flavoring to adjust the taste.

Embodiment 1:

Prepare the compound from the prepared ingredients with the following recipe:

Extract of magnolia bark	0.14 kg
Dietary fiber	30 kg
Fat	2.5 kg
Stevia sweetener microcapsules	0.8 kg
Gum base	25 kg
Granulated sugar	31 kg
Glucose syrup	7.86 kg
Glycerol	2 kg
Flavorings	0.7 kg

Place the gum base, dietary fiber and fat into the mixer and mix to homogeneity.

Add the extract of magnolia bark, stevia sweetener microcapsules and other ingredients. Process the mixture by extrusion, cutting and packaging to obtain the final product.

Embodiment 2:

Prepare the mixture from the prepared ingredients with the following recipe:

Extract of magnolia bark	0.25 kg
Dietary fiber	40.3 kg
Fat	3 kg
Stevia sweetener microcapsules	1.2 kg
Gum base material	25 kg
Granulated sugar	18.3 kg
Glucose syrup	10.15 kg
Glycerol	1 kg
Flavorings	0.8 kg

The remaining steps are the same as in Embodiment 1.

Embodiment 3:

Prepare the mixture from the prepared ingredients with the following recipe:

Extract of magnolia bark	1 kg
Dietary fiber	63 kg
Fat	2.5 kg
Microcapsules of stevia sweetener	2 kg
Gum base	20 kg
Glucose syrup	8.5 kg
Glycerol	2 kg
Flavorings	1 kg

The remaining steps are the same as in Embodiment 1.

For the anticaries chewing gum made on the basis of the above embodiments, each stick of chewing gum should be 3-6 g in weight, preferably 5 g. The stick can be chewed 3 times a day after meals (or more or less frequently as desired) for a duration of 5-10 minutes.

[19]中华人民共和国专利局

[11] 公开号 CN 1096699A



[12] 发明专利申请公开说明书

[21]申请号 94110006.5

[51]Int.Cl⁵

A61K 35/78

[43]公开日 1994年12月28日

[22]申请日 94.1.7

[71]申请人 沈阳市红旗制药厂

地址 110041辽宁省沈阳市大东区新龙街36号

[72]发明人 杨 哲

[74]专利代理机构 沈阳市专利事务所

代理人 刁佩德 贾世明

A61K 9/68 A23G 3/30

RECORD COPY
CENTRAL FILE

说明书页数:

附图页数:

[54]发明名称 防龋口胶及其制备方法

[57]摘要

本发明涉及一种防龋口胶及其制备方法,所用原料中药厚朴提取物、甜菊糖微囊、植物纤维素、油脂、胶基及辅料等,放入搅拌机中混匀、捏和、轧制切块,包装即为成品。它制备方法简便、食用方便,除具有一股香口胶的优点外,还具有洁齿灭菌、防龋效果显著的特点。

(BJ)第 1456 号